DECLARATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Takahiro ITO et al.
Serial No. 10/509,912: Group Art Unit: 1623
Filed: October 4, 2004: Examiner: Jonathan S. Lau
For: LIQUID PREPARATION COMPRISING CAMPTOTHECIN DERIVATIVE AND PHARMACEUTICAL COMPOSITION PRODUCIBLE BY LYOPHILIZING THE PREPARATION

Honorable Commissioner for Patents
Sir:

[A] I, Yasuhiro SHINDO, a citizen of Japan residing 106-1405, Itomachi, Chuo-ku, Kobe-shi, Hyogo-ken, Japan, declare as follows:

I graduated from the faculty of agriculture of Kobe University in March, 1983, and completed the post-graduate/master course of agricultural chemistry of Kobe University in March 1985.

Since April, 1985, I have been an employee of Mitsubishi Tanabe Pharma Corporation (Former Tanabe Seiyaku Co. Ltd.), 2-10 Dosho-machi 3-chome, Chuo-ku, Osaka, Japan and I am presently in charge of manager of Patent Group 1, Intellectual Property Department of the company.

I am familiar with the subject matter of the invention in this U.S. Serial No. 10/509,912.

[B] I have studied the paper from the literature cited below and the summarized data of T-0128-containing solutions disclosed therein as presented in the form of an Attachment (two pages):

"HARADA, Mitsunori et al. Title: Determinants for drug release from T-0128, camptothecin analogue-carboxymethyl dextran conjugate, Journal of Controlled Release 69 (2000) 399-412."

I hereby submit this Declaration into evidence in the present application.

[C] I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or

imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

This 8th day of August, 2008

Yasuhiro SHINDO

(Attachment)

Appendix: T-0128-containing solution disclosed in Harada et al.

1. Solutions for In vitro Drug Release Tests (Paragraph 2.4 of Harada et al.)

1.1. Solution for hydrolysis stability of T-0128 peptidyl linker to the liver lysosome or homogenate

T-0128 content	100 □g.mL (5 □g.mL of T-2513)
pH	4
w/v % of T-0128	0.01
Buffer (mM)	acetate (40)
$CaCl_2$	Nill
EDTA	1 mM
Reduced Glutathione	5 mM
Triton X-100	0.1 w/w %

1.2. Solutions for hydrolysis stability of T-0128 to various types of pure enzymes (See Table 1 of Harada et al.)

1.2.1. Solutions for Serine proteinases and Metalloproteinases

T-0128 content: 100 □g.mL (5 □g.mL of T-2513)					
pH	3	4	5	6	7
w/v % of T-0128	0.01	0.01	0.01	0.01	0.01
Buffer (mM)	acetate (40)	acetate (40)	acetate (40)	phosphate (40)	phosphate (40)
$CaCl_2$	10 mM	10 mM	10 mM	10 mM	10 mM
EDTA					
Reduced Glutathion					

1.2.2. Solutions for Cystine proteases

T-0128 content: 100 μg.mL (5 μg.mL of T-2513)					
pH	3	4	5	6	7
w/v % of T-0128	0.01	0.01	0.01	0.01	0.01
Buffer (mM)	acetate (40)	acetate (40)	acetate (40)	phosphate (40)	phosphate (40)
$CaCl_2$					
EDTA	1 mM	1 mM	1 mM	1 mM	1 mM
Reduced Glutathione	5 mM	5 mM	5 mM	5 mM	5 mM

1.2.3. Solutions for Aspartic proteinases

T-0128 content: 100 μg.mL (5 μg.mL of T-2513)					
pH	3	4	5	6	7
w/v % of T-0128	0.01	0.01	0.01	0.01	0.01
Buffer (mM)	acetate (40)	acetate (40)	acetate (40)	phosphate (40)	phosphate (40)
$CaCl_2$					
EDTA					
Reduced Glutathione					

2. Solutions for In vivo inhibition studies (Paragraph 2.5 of Harada et al.)

T-0128 content: 10 mg.mL (0.5 mg.mL of T-2513)	
pH	Not disclosed
w/v % of T-0128	1.0
Buffer	Nill (Solvent: saline)